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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,931	07/25/2003	Dean A. Klein	54459-277675	5405

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PATENT DOCKETING
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EXAMINER	
JASANI, ASHISH S	

ART UNIT	PAPER NUMBER
3737	

DATE MAILED: 09/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,931	KLEIN ET AL.	
	Examiner	Art Unit	
	Ashish S. Jasani	3737	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :06/20/2005, 01/10/2005, 12/01/2003, 06/23/2004, 12/08/2003, and 11/17/2003.

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statements received on 06/20/2005, 01/10/2005, 12/01/2003, 06/23/2004, 12/08/2003, and 11/17/2003 acknowledged. The information disclosure statement meets the requirements of 37 CFR 1.97 and 37 CFR 1.98, and therefore the reference listed therein have been considered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-32, and 42-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klein (USPN 6394965) in further view of Watkin et al. (Acad Radiol 2002; 9(suppl 2):S285–S289).

With regards to claims 1, 2, 4-13, 22, 23, 24, 27, 42, 49-56, 70, and 77; Klein teaches of tissue marking using microparticles (abstract). Klein teaches of "implanting at least one permanent marker" such that "delivery of microparticles using a needle and syringe allows very precise delivery of microparticle markers to a desired tissue site, this is particularly true if a biopsy probe used to perform a biopsy is used to assist delivery of microparticles for tissue marking, without first moving the biopsy sheath" (column 2, lines 54-59). Klein teaches of imaging such that "the detectable component, e.g.,

contrast-enhancing agent, can be any material capable of enhancing contrast in a desired imaging modality (e.g. magnetic resonance, X-ray, ultrasound, magnetotomography, electrical impedance imaging, light imaging (e.g. confocal microscopy and fluorescence imaging) and nuclear imaging (e.g. scintigraphy, SPECT and PET))" (column 4, lines 6-13). Klein teaches of treating the site such that "the invention provides methods of marking tissue for any reason, such as to mark the site of the removal of a tissue, e.g., the removal of a polyp from a colon or rectum; to mark the site of a biopsy, including a breast biopsy, a prostate biopsy, a colon biopsy, a rectum biopsy; or to mark the site of any other medical procedure or removal of tissue or biopsy at another tissue location" (column 3, lines 52-58). Klein teaches that the contrast enhancement can be for a number of imaging modalities, but does not teach that the contrast agent is multimodal.

Watkin et al. teaches of a multimodal contrast agent for use in MRI, X-ray or CT, and ultrasound such that "Our preliminary research suggests that Gd2O3 sequestered within albumin microspheres can significantly improve the echogenicity of protein microspheres. In addition, the non-chelated interaction of Gd2O3 with mobile protons (15), potential for physical rotation of Gd2O3 (16), and decreased tumbling rate of Gd2O3 when associated with (macromolecular) albumin microspheres are all mechanisms which are anticipated to contribute to GOAM's usefulness as a T1 and T2 relaxation enhancing contrast agent for MR imaging. Lastly, imaging of GOAM, a protein microsphere contrast agent that contains multiple gadolinium oxide particles, each of which are made up of several gadolinium atoms per molecule, will permit

enhanced CT imaging due to the high atomic weight and high k-edge of gadolinium" (page S289, ¶ 2).

It would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to combine the Klein biopsy marking method with the Watkin et al. multimodal contrast agent to enhance diagnosis with multiple imaging modalities.

With regards to claim 3,

With regards to claims 14, 17-19, 21, and 25; Klein teaches of monitoring such that "The tissue may be marked for any reason, for example to return to the same tissue site to monitor the progress of a medical condition or a treatment, or to perform a subsequent biopsy at the same site" (column 3, lines 58-62).

With regards to claims 15, 16, and 26; Klein teaches of mapping and radiation therapy such that " the tissue may be marked to provide a target for radiation treatment, i.e., detectable microparticles can be delivered to a tissue site to act as a target at which or near a beam of radiation can be precisely directed" (column 3, lines 62-65).

With regards to claim 20, Klein teaches of guiding such that "the tissue may be marked for any reason, for example to return to a the same tissue site to monitor the progress of a medical condition or a treatment, or to perform subsequent biopsy" (column 3, lines 58-61).

With regards to claim 28, Watkin et al. teaches of MRI, CT, and ultrasound which can all be electronic portal imaging; Watkin et al. teaches of CT or X-ray which can be portal film imaging.

With regards to claims 29-32 and 78, Klein teaches of a "biologically active agent" of beta-glucan such that "the microparticles can be delivered using a fluid carrier, which can be any biologically compatible material capable of delivering the microparticles to a desired tissue site, such as a biologically compatible suspension, solution, or other form of a fluid or gel" (column 2, lines 41-45. Klein goes on to teach of the carrier being that of beta-glucan (column 8, lines 58-61).

With regards to claim 42, Klein teaches of implanting a marker (column 2, lines 10-23), imaging from a number of modalities (column 3, lines 34-41), and treatment (column 3, lines 51-65).

With regards to claim 43-44, Klein teaches of monitoring the treatment site such that "the tissue may be marked for any reason, for example to return to a the same tissue site to monitor the progress of a medical condition or a treatment, or to perform subsequent biopsy" (column 3, lines 58-61). A biopsy is a removal of tissue.

With regards to claim 45, Klein teaches of breast biopsy (column 3, line 54) in which it is well known in the art that it can be imaged via MRI, CT or X-Ray, and Ultrasound.

With regards to claim 57-59, Klein et al. teaches of aluminum oxide and zirconium oxide (column 2, lines 37-40).

With regards to claims 60-63 and 73, Klein teaches of a biocompatible pyrolytic carbon surface (abstract).

With regards to claim 64-66, Klein teaches that the particles can have a size of 1000 microns (column 2, lines 17).

With regards to claims 67-68, Watkin et al. teaches of a microbubble which is spherical and hollow.

With regards to claim 69,

With regards to claim 71, Klein teaches that the particle can be radiopaque (column 2, line 21).

With regards to claim 72, Klein teaches of additional material such that "Preferred paramagnetic metals include Gd (III), Dy (III), Fe (II), Fe (III), Mn (III) and Ho (III), and paramagnetic Ni, Co and Eu species. Preferred heavy metals include Pb, Ba, Ag, Au, W, Cu, Bi and lanthanides such as Gd, etc." (column 4, lines 57-60).

With regards to claim 74-76, Klein teaches of a beta-glucan suspension carrier which is biocompatible and derived from cell walls (column 8, lines 45-47).

4. Claims 33 - 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klein (USPN 6394965) in further view of Watkin et al. (Acad Radiol 2002; 9(suppl 2):S285–S289) and in further view of official notice.

Klein teaches of tissue marking using microparticles (abstract). Klein teaches of "implanting at least one permanent marker" such that "delivery of microparticles using a needle and syringe allows very precise delivery of microparticle markers to a desired tissue site, this is particularly true if a biopsy probe used to perform a biopsy is used to assist delivery of microparticles for tissue marking, without first moving the biopsy sheath" (column 2, lines 54-59). Klein teaches of imaging such that "the detectable component, e.g., contrast-enhancing agent, can be any material capable of enhancing

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Watkin et al. teaches of a multimodal contrast agent for use in MRI, X-ray or CT, and ultrasound such that "Our preliminary research suggests that Gd2O3 sequestered within albumin microspheres can significantly improve the echogenicity of protein microspheres. In addition, the non-chelated interaction of Gd2O3 with mobile protons (15), potential for physical rotation of Gd2O3 (16), and decreased tumbling rate of Gd2O3 when associated with (macromolecular) albumin microspheres are all mechanisms which are anticipated to contribute to GOAM's usefulness as a T1 and T2 relaxation enhancing contrast agent for MR imaging. Lastly, imaging of GOAM, a protein microsphere contrast agent that contains multiple gadolinium oxide particles, each of which are made up of several gadolinium atoms per molecule, will permit

enhanced CT imaging due to the high atomic weight and high k-edge of gadolinium" (page S289, ¶ 2).

The examiner takes official notice that multimodal image fusion is well known in the art. The practice commonly fuses structural images (x-ray or CT) with functional images (MRI, PET, SPECT, or US) by using either structural marker or statistical information to register the images.

It would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to combine the Klein biopsy marking method with the Watkin et al. multimodal contrast agent and with multimodal image fusion to enhance diagnosis with multiple imaging modalities by offering both structural and functional imagery of the treatment site.

With regards to claims 39-41, Klein teaches of performing radiation therapy (column 3, lines 62-65).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ashish S. Jasani whose telephone number is 571-272-8025. The examiner can normally be reached on Mon. - Fri. 9:30 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Casler can be reached on (571) 272 - 4956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ASJ

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